REMARKS

In the Action, claims 1-20 are rejected, and claims 21-32 are withdrawn from consideration as being directed to the non-elected invention. In response, claims 5, 16 and 20 are amended to correct matters of form noted in the Action.

In view of these amendments and the following comments, reconsideration and allowance are requested.

The Rejections

Claims 1, 2, 7 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 02/083194. WO '194 is cited for disclosing a biostructure having an internal microstructure with a bimodal pore size.

WO '194 does not disclose or suggest the granulates of the claimed invention or shaped articles formed from granulates having a statistically distributed porosity with the discrete pore size ranges as recited in the claims. The present invention is particularly directed to granulates or shaped pieces from the granulates or shaped pieces form the granulates having a statistical pore size distribution, polygonal formed pores, as well as polygonal formed granulates.

WO '194 discloses a regular biostructure, and thus, is a shaped piece referred to as an engineering or shaped article. This results in a shaped article having a specific and regular form.

WO '194 discloses a bimodal pore size distribution having different size ranges that are not discrete pore size ranges as in the claimed invention. Claim 1 specifically recites that only the inner connecting pore share of the porosity of the particles has a pore size less than 10 μm. Thus, the particles are interconnected by a pore share having a pore size of less than 10 μm. Claim 1 further recites the porosity having an irregular geometric shape and where

the sintered particles of the calcium phosphate have a particle size smaller than 63 μm and a D_{50} value in the range of 5 to 20 μm. The D_{50} value refers only to 50% of the particles having a particle size below this value and 50% of the particles having a particle size above the value and has no relation to the average particle diameter ranges. WO '194 clearly fails to disclose sintered particles of calcium phosphate having a particle size smaller than 63 μm and a D_{50} value in the range of 5 to 20 μm. Furthermore, the particle size range disclosed in WO '194 does not inherently satisfy the features of claim 1.

WO '194 further fails to disclose the discrete pore size distribution having pore diameters in the range of 0.5 to 10 μm and a second pore diameter of 10 to 100 μm as in claim 2. As noted in the Action, WO '194 only discloses the pore sizes being greater than 10 μm. Thus, WO '194 does not disclose either expressly or inherently the claimed two discrete pore size distributions.

WO '194 also fails to disclose the bone formation agent in the form of a granulate where the granulate has a particle size of 50 to 10,000 μm. WO '194 discloses a biostructure built from particles having a size of 10 to 50 μm up to 300 μm. The biostructure of WO '194 is not in the form of a granulate as in the claimed invention. The granulate of the claimed invention is different from the biostructure of WO '194. WO '194 further fails to disclose the claimed antibacterial, wound healing promoting agents, bone growth promoting agents, and anticoagulant substances on the surface or in the internal pore structure of the granulate particles of the present invention as recited in claim 17.

In view of the above comments, the claims are not anticipated by WO '194.

Claims 1 and 3-4 are rejected under 35 U.S.C. § 103(a) as being obvious over WO '194 in view of WO 92/21302. WO '302 is cited for disclosing an implant having three different pore sizes.

The claimed invention has three discrete pore size ranges which are statistically distributed in the bone formation material. As recited in claims 3 and 4, the pores are distributed to have a maxima of three discrete pore size distributions having a pore diameter in the range of 0.5 to 10 μm, 10 to 100 μm, and 100 to 5,000 μm. Claim 4 specifically recites that 20 to 40% by volume of the pore size distribution of pore diameters in the range of 0.5 to 10 μm and 5 to 40% by volume of the pore size distribution having a pore diameter in the range of 10 to 100 μm and 1 to 40% by volume of the pore size distribution having a pore diameter in the range of 100 to 5,000 μm where the overall porosity does not exceed 85% by volume. The claimed pore size distribution is essential to the function of the present invention. WO '302 does not disclose or suggest these features. WO '302 discloses "not more than 5%" of the pore size when in the range of 10 to 50 μm.

As noted above, the micropores having a pore size less than 10 μm connect the other two pore distributions. Thus, the claimed pore size distribution having a pore diameter in the range of 0.5 to 10 μm define the interconnecting pore system. See, for example, page 9, third paragraph of the specification which discloses the interconnecting macropore network having an upper limit of 10 μm for interconnecting the pore system. See, also, page 10, first paragraph of the specification. The interconnecting macropore system of the invention is accessible from the surface and may be a shelter for microorganisms which may not be reached by a systemic treatment with antibiotics. Therefore, it is essential for the present invention that the proportion of the interconnecting pores be less than 10 μm as disclosed on page 8, first full paragraph of the specification. Furthermore, the pore size is dependent on the size of the granulate.

The pores of the present invention are statistically distributed over the whole material. WO '302 discloses the pore size ranges which are distributed on different parts of the implant but are not distributed throughout the article as in the present invention. Thus, it would not

have been obvious to one of ordinary skill in the art to provide the claimed bone formation agent having the claimed discrete pore size distribution of claims 3 and 4 in view of WO '302 and WO '194.

Claims 5, 8-16 and 18-20 are rejected as being obvious over WO '194 in view of WO '302 and further in view of U.S. Patent No. 6,521,246 to Sapieszko et al. Sapieszko et al. is cited for disclosing inorganic shaped bodies useful for bone grafting materials.

The dependent claims are allowable as depending from an allowable base claim and for reciting additional features of the invention. Sapieszko et al. does not suggest to one of ordinary skill in the art the calcium phosphate of claim 5, the non-uniform granulate of claim 8, the uniform granulate of claim 9, or the spherical granulate of claim 10, in combination with the features of claim 1. Sapieszko et al. is directed to inorganic shaped bodies from beta-tricalcium phosphate having a porosity of 30 to 90%. The pores are described as being substantially uniform and the method disclosed in the Examples describe a template technique in which a sponge is used as the substrate. The sponge of Sapieszko et al. is imbibed with a reaction solution containing calcium phosphate. The organic portion of the sponge is burned to leave a calcium phosphate framework in the form of a sponge. See, for example, Example 51. The pores of the sponge normally have a round shape as shown in the Figures.

In contrast, the claimed invention is directed to granulates and/or shaped bodies having a porosity of up to 80% having three discrete pore size ranges. Furthermore, only the pore size below 10 μm interconnects the other pores as discussed above.

In the present invention, the pores are statistically distributed and are not round as in Sapieszko et al. The pores of the present invention have an irregular geometrical shape and have a particle size having a specifically defined range. The particle size range of the claimed invention is not a random selection but has a specific purpose. The primary particle

size is selected so that the size thereof is greater than the size required for the access of macrophages. Thus, the risk of septic foreign body reactions, which are caused by small particles which might be decomposed by macrophages, is reduced. See, for example, page 5, fourth paragraph of the specification. In addition, the need for a stable sintered framework exists to prevent fine abrasion during mechanical stress which could also result in foreign body reactions.

Sapieszko et al. does not disclose or suggest the necessity of the claimed granulates or avoiding abrasion by stronger sintered framework. The D_{50} value of the claimed particles is also not disclosed or inherent in Sapieszko et al. Based on the production method disclosed in Sapieszko et al., one skilled in the art would recognize that the product produced by the method is a very fine grained product as shown in Figure 22 of Sapieszko et al.

The cited patents either alone or in combination do not suggest to one of ordinary skill in the art the claimed discrete pore size distributions, only the micropores of 10 μm or less interconnecting the pores, the large primary particles, the irregular geometric shapes of the pores or the mechanically stable sintered framework. Accordingly, the claims are not obvious over the combination of the cited patents.

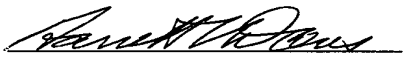
The combination of the cited patents further fails to disclose the maxima of the pore size distributions matched to the granulate size as in claim 11, the maxima of the pore size distributions being less than half of the average granulate size of the granulate fraction in the range of 10 to 50% as in claim 12, the statistical porosity in the form of tubular pores as in claims 14 and 15, the compact shaped body having a pore size distribution as defined in claim 16, or the shapes of claims 18 and 20, in combination with the features of claim 1.

Claims 1 and 6 are rejected as being obvious over WO '194 in view of the article by Trisi et al. Trisi et al. is cited for disclosing the use of beta-tricalcium phosphate in bone regeneration.

Trisi et al. shows a material having a microporosity of 35% and does not disclose or suggest a material having at least two discrete pore size ranges as defined in the claimed invention. The pore size, width of the pores, and the pore structure as defined in the claimed invention are not disclosed or suggested in Trisi et al. Thus, it would not have been obvious to one of ordinary skill in the art to form irregular shaped pores, have a limited primary particle size, a phase purity and interconnecting pore sizes of less than 10 μm as in claim 6 and claim 1 in view of WO '194 and Trisi et al.

In view of these amendments and the above comments, the claims are submitted to be allowable over the art of record. Accordingly, reconsideration and allowance are requested.

Respectfully submitted,



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